REMARKS

Applicants believe that no new matter is introduced in the filing of this Preliminary Amendment. Applicants respectfully request examination of the above-named application in view of the present amendments.

Respectfully submitted,

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APPENDIX A
MARKED-UP VERSION OF PARAGRAPHS
(as amended September 19, 2001)

In accordance with 37 C.F.R. § 1.121(b), Applicants submit herewith a marked-up version of the insert as the first paragraph on page one of the specification, in order to indicate the changes Applicants have made to this paragraph.

This application is a continuation of International Application PCT/US00/07089 filed March 20, 2000, the disclosure being incorporated herein by reference in its entirety. This application is based on U.S. Provisional applications 60/139,484 filed March 19, 1999, 60/138,578 filed June 11, 1999 and 60/155,485 filed September 23, 1999.

APPENDIX B
MARKED-UP VERSION OF CLAIMS
(as amended September 19, 2001)

In accordance with 37 C.F.R. § 1.121(b), Applicants submit herewith a marked-up version of the claims in order to indicate changes Applicants have made to these claims.

Please delete claims 1-19 and add new claims 20-35 as follows.

20. (New) A method of increasing cerebral bioavailability of a physiologically active composition in an individual comprising administering an NO-increasing agent or agents to the individual in need of enhanced drug delivery, wherein said agent is administered substantially contemporaneously with the physiologically active composition whose delivery is to be enhanced and said agent or agents increases the production of NO by preexisting ecNOS.

21. (New) A method of increasing cerebral bioavailability of a physiologically active composition in an individual comprising introducing the composition into the blood stream of the individual substantially contemporaneously with a blood flow enhancing amount of L-arginine.

22. (New) A method of increasing cerebral bioavailability of a physiologically active composition in an individual according to claim 20 comprising introducing the composition into the blood stream of the individual substantially contemporaneously with a blood flow enhancing amount of an agent which increases the production of NO by preexisting ecNOS and at least one other NO-increasing agent.

23. (New) The method according to claims 20 and 22, further wherein the agent which increases the production of NO by preexisting ecNOS is selected from the group consisting of L-arginine, NADPH, and tetrahydrobiopterin.

24. (New) The method according to claim 23, further wherein the agent which increases the production of NO by preexisting ecNOS is L-arginine.

25. (New) The method according to claim 22, wherein the agent which increases the production of NO by preexisting ecNOS is L-arginine and the at least one other NO-increasing agent is a different an agent which increases the production of NO by preexisting ecNOS.

26. (New) The method according to claim 22, wherein the agent which increases the production of NO by preexisting ecNOS is L-arginine and the at least one other NO-increasing agent is a non-ecNOS NO-generating system.

27. (New) The method according to any one of claims 20 to 22 wherein the individual in need of enhanced drug delivery has experienced, is experiencing, or is at abnormally elevated risk of experiencing an ischemic stroke.

28. (New) The method according to any one of claims 20 to 22 wherein the physiologically active composition has a site of action in the brain.

29. (New) A composition for increasing cerebral bioavailability of a physiologically active composition in an individual comprising a blood-flow enhancing amount of an NO-increasing agent or agents which increases the production of NO by preexisting ecNOS and the physiologically active composition.

30. (New) The composition according to claim 29, wherein the NO-increasing agent comprises an agent which increases the production of NO by preexisting ecNOS and at least one other NO-increasing agent.

31. (New) The composition according to claim 29 or claim 30, wherein the agent which increases the production of NO by preexisting ecNOS is selected from the group consisting of L-arginine, NADPH, and tetrahydrobiopterin.

32. (New) The composition according to claim 29 or claim 30, wherein the agent which increases the production of NO by preexisting ecNOS is L-arginine.

33. (New) The composition according to claim 30, comprising L-arginine and at least one other NO-increasing agent which is a different an agent which increases the production of NO by preexisting ecNOS.

34. (New) The composition according to claim 30, comprising L-arginine and at least one NO-increasing agent which is a non-ecNOS NO-generating system.

35. (New) The composition according to claim 29 or claim 30, wherein the physiologically active composition has a site of action in the brain.